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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,409	01/23/2002	Maria Palasis	104914.132US2	1618

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EXAMINER	
KELLY, ROBERT M	
ART UNIT	**PAPER NUMBER**
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/057,409	PALASIS, MARIA	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-11,15-22,24-38,40-48 and 52-54* is/are pending in the application.

4a) Of the above claim(s) *4-11,16,18,20-22,25-37,41-48,52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,17,19,24,25,38,40 and 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/8/06, requesting entry and examination of the submission of 9/13/06 has been entered.

Claims 23, 50, and 51 are cancelled.

Claims 15, 17, 19, and 38 are amended.

Claims 4-11, 15-22, 24-38, 40-48, and 52-54 are presently pending.

Election/Restrictions

In keeping with the prior restriction requirement, Claims 15, 17, 19, 24-25, 38, 40, and 54 are presently considered, with respect to the elected invention.

Claim Status, Cancelled Claims

In light of Applicant's cancellation of Claims 23, 50, and 51, all rejections and/or objections to such claims are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

While the rejections for enablement for any cell type, delivery not adjacent to ischemic tissue are withdrawn, Claims 15, 17, 19, 23-25, 38, 40, 50-51, and 54 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the intramyocardial delivery of autologous or allogenic mesenchymal stem cells modified *ex vivo* to express an angiogenic factor via a constitutive promoter operatively linked to a sequence encoding an angiogenic factor, to normal tissue adjacent to ischemic tissue in the myocardium, does not reasonably provide enablement for the absence of a transgene, or any non-constitutive promoters, for reasons of record, and as modified below in the response to argument.

Response to Argument – Enablement

Applicant's argument of 9/21/05, submitted for reconsideration, have been fully considered but are not found persuasive.

With regard to the several bases of rejection withdrawn, the arguments relevant to such are not addressed, as they are deemed overcome by the argument and amendment provided.

Applicant argues that the specification is enabling of any non-autologous stromal cells because the art demonstrates several transplanted non-autologous organs (pp. 9-10).

Such is persuasive for the use of non-autologous, but not xenogenic tissues. It is well known that xenogenic tissues garner much larger rejections compared to that of autologous and allogenic transplantations. To wit, with regard to non-allogenic transplantation of cells *Game et*

al (Wien Klin Wochenschr 2001;113:823-38) detailed different types of allogenic and xenogenic rejection (hyperacute, acute, chronic) and underlying mechanisms involving multiple pathways that lead to the failure of allogenic and xenogenic transplantation, and states, "WHILE MAJOR IMPROVEMENTS HAVE BEEN MADE IN THE PREVENTION AND TREATMENT OF HYPERACUTE AND ACUTE TRANSPLANT REJECTION, MOST GRAFTS WILL SUCCUMB TO CHRONIC REJECTION: THIS REFLECTS THE EXTENT OF OUR KNOWLEDGE OF THE MECHANISMS THAT DRIVE THESE PROCESSES", as for xenotransplantation, "NOVEL APPROACHES HAVE OVERCOME SOME EARLY ANTIBODY MEDIATED REJECTION EVENTS BUT THEN REVEAL A HUGE, INTENSE, ADAPTIVE CELLULAR RESPONSE". Hence, other than autologous and allogenic transplantation, no other form of transplantation is reasonably predicted to work.

With regard to the absence of any disclosure as to any other *ex vivo* modification other than the use of a transgene encoding the angiogenic factor, Applicant appears to generally argue that they are simply claiming the use of a transgene placed within the cells (e.g., p. 12, paragraph 2). However, the claims encompass any *ex vivo* modification, which is much broader than the only described *ex vivo* modification: transformation to express an angiogenic transgene. Hence, the specification still fails to enable any other method of *ex vivo* modification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 15, 17, 19, 24, 25, 38, 40 and 54 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 7,097,832 to Kornowski, et al., Patented 8/29/06, and claiming priority to at least 8/5/00.

With regard to Claims 15, 17, 19, and 38, Kornowski teaches treatment of myocardial conditions with administration of autologous bone marrow (e.g., ABSTRACT), which may carry a transgene for an angiogenic growth factor, including HIF-1 (e.g., ABSTRACT; col. 2, paragraph 6). The bone marrow cells which may be transformed include the stromal cells (e.g., col. 16, paragraph 2). Further, the cells may be administered to tissue adjacent ischemic tissue (e.g., col. 15, paragraph 4). Such may be done to increase collateral blood vessel formation (e.g., col. 1, paragraph 2) and induce angiogenesis (e.g., col. 2, paragraph 3), and increase contractile function (e.g., EXAMPLE 4), in an ischemic heart myocardium (e.g., col. 2, paragraph 6). Moreover, the cells are modified to comprise the transgene *ex vivo* with e.g., a plasmid or adenoviral vector comprising the angiogenic transgene (e.g., col. 16, paragraph 2). Lastly, such HIF-1 production increases VEGF levels produced by the cells (e.g., col. 16, paragraph 2 and Claim 8), thereby modifying the cells to produce multiple angiogenic factors, including HIF-1 and VEGF.

With regard to Claims 24 and 40, the cells may be injected into multiple sites, including multiple sites adjacent to the ischemic zone (e.g., EXAMPLE 4).

With regard to Claim 54, the injection may be made by catheter (e.g., col. 10, paragraph 2).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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